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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/544,254	08/23/2005	Mizuo Miyazaki	3190-081	1342

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KILYK & BOWERSOX, P.L.L.C.
400 HOLIDAY COURT
SUITE 102
WARRENTON, VA 20186

EXAMINER	
AUDET, MAURY A	
ART UNIT	PAPER NUMBER
1654	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

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Office Action Summary	Application No.	Applicant(s)	
	10/544,254	MIYAZAKI ET AL.	
	Examiner	Art Unit	
	Maury Audet	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 August 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/05, 4/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6, 8, 10-11, and 19-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Powers et al. (US 5,543,396; also cited in IDS of 04/23/04, P5).

Powers et al. teach a pharmaceutical composition in any form (inherently containing a high molecular weight carrier, diluent or excipient since can be in the form of e.g. tablet, aqueous or oily suspension, etc.) (col. 16, lines 23-40), comprising protease inhibitors such as Suc-Val-Pro-Phe^{P}(Oph)$_2$ (e.g. Example 17), described as the "best inhibitor for [serine proteases] chymotrypsin and chymotrysin-like enzymes" (col. 5, lines 40-44; col. 3, lines 50-53), which are involved in "tissue remodeling" [e.g. tissue adhesion formation] (col. 1, lines 41-43) [which Applicant also describes this compounds as a chymase inhibitor, e.g. claim 6, rendering this compounds a dual labeled/acting serine protease/chymase inhibitor].

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Powers et al. (US 5,543,396; also cited in IDS of 04/23/04, P5) in view of Scharpe et al. (US 2002/0061839 A1). [Although the claims are to products, there are nevertheless intended use limitations therein to which the present rejection is made under 103, as well as to claim 7, as to the obviousness of selecting other known serine protease/chymase inhibitors for use in the present medicament product].

Powers et al. is discussed above. Powers et al. teach a pharmaceutical composition in any form (inherently containing a diluent or excipient since can be in the form of e.g. tablet, aqueous or oily suspension, etc.) (col. 16, lines 23-40), comprising protease inhibitors such as Suc-Val-Pro-Phe^{p}(Oph)$_2$ (e.g. Example 17), described as the "best inhibitor for [serine proteases] chymotrypsin and chymotrysin-like enzymes" (col. 5, lines 40-44; col. 3, lines 50-53), which are involved in "tissue remodeling" [e.g. tissue adhesion formation] (col. 1, lines 41-43). However, Powers et al. does not expressly teach the use all protease inhibitors or protease inhibitors such as Suc-Val-Pro-Phe^{p}(Oph)$_2$ to reduce [tissue] adhesion formation (e.g. claim 1) or all the various forms of administration (e.g. claim 25-30, such as liposomes).

Scharpe et al. teach the use of serine protease inhibitors such as Suc-Val-Pro-Phe (para 69) in virtually any pharmaceutical admixture/formulation, such as liposomes (para 125).

It would have been obvious to one of ordinary skill in the art at the time of the invention to use any protease inhibitor, such as Suc-Val-Pro-Phe^{p}(Oph)$_2$, to reduce [tissue] adhesion formation as one of the methods relevant to inhibiting the actions of the serine protease chymotrypsin methods in Powers et al., because Powers et al. advantageously teaches the use of protease inhibitors such as Suc-Val-Pro-Phe^{p}(Oph)$_2$ to inhibit chymotrysin, which is a serine

protease known to be used in the pathway of tissue remodeling (e.g. adhesion/ aggregation/binding), like other protease inhibitors within the family of protease inhibitors, and one of skill in the art would recognize that administering protease inhibitors such as Suc-Val-Pro-Phe^{p}(Oph)$_2$, even if not expressly stated, is administered in part or total to combat such tissue adhesion caused by chymotrypsin.

It would have been obvious to one of ordinary skill in the art at the time of the invention to put protease inhibitors such as Suc-Val-Pro-Phe^{p}(Oph)$_2$ in any formulation/admixtures (e.g. any "transmitter" such as any carrier molecule having high molecular weight such as hyaluronic acid, hydrogel, carboxymethylcellulose, dextran, cyclodextran; e.g. Applicant's claims 9, 12-18) in the composition of Powers et al, because Scharpe et al. advantageously teach that serine protease inhibitors may be put in composition with e.g. liposomes, etc. depending on the desired result/administration route; just as Powers et al. likewise discussed in terms of motivation for route/type of administration being left open to the skilled artisan and the desired effect when using protease inhibitors.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-20 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7, 10-12, 30, and 33 of copending Application No. 10/602,035 (Miyazaki et al., also with this Examiner). Although the conflicting claims are not identical, they are not patentably distinct from each other because '035 expressly claimed, though through different choice of words, the same invention/compounds/medicament, including the preferred protease inhibitors such as Suc-Val-Pro-Phe^{p}(Oph)$_2$, for the purpose of inhibiting tissue adhesion.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 U.S.C. § 112 1st Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention..

Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for reducing adhesion formation (as well as postoperatively) between tissue surfaces (see specification throughout) using protease inhibitors (e.g. Suc-Val-Pro-Phe^{p}(Oph)$_{2}$), for a period of time sufficient to reduce adhesion formation; does not reasonably provide enablement for *preventing* adhesion formation between tissue surfaces using protease inhibitors such as Suc-Val-Pro-Phe^{p}(Oph)$_{2}$. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicants have reasonably demonstrated/disclosed that the claimed sequences may be used for reducing adhesion formation between tissue surfaces using protease inhibitor such as Suc-Val-Pro-Phe^{p}(Oph)$_{2}$, for a period of time sufficient to reduce adhesion formation; and/or reducing the risk thereof. However, the claims also encompass using the claimed composition to prevent adhesion formation between tissue surfaces using protease inhibitor such as Suc-Val-Pro-Phe^{p}(Oph)$_{2}$, which is clearly beyond the scope of the instantly disclosed/claimed invention. Please note that the term "prevent" is an absolute definition which means to stop from occurring and, thus, requires a higher standard for enablement than does the term "treat", especially since it is notoriously well accepted in the medical art that the vast majority of afflictions/disorders

suffered by mankind cannot be totally prevented with current therapies (other than certain vaccination regimes) - including preventing such disorders as ordinary tissue adhesion (which clearly is not recognized in the medical art as being a totally preventable phenomenon/condition).

Accordingly, it would take undue experimentation without a reasonable expectation of success for one of skill in the art to make and/or use the claimed composition which would function to prevent prevent adhesion formation between tissue surfaces using protease inhibitors such as Suc-Val-Pro-$Phe^{p}(Oph)_2$.

Claim Rejections - 35 USC § 112 2nd

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6-8 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). The term "L" in claim 8 to describe the amino acid Phe is used by the claim to mean "L form", while the accepted meaning is "that all peptides are in native L form, absent evidence to the contrary (in

which case the alternative D form is listed." The term is indefinite because the specification does not clearly redefine the term. Thus, the 3 compounds of claim 6 and 8 are deemed the same compound, in L form.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maury Audet whose telephone number is 571-272-0960. The examiner can normally be reached on M-Th. 7AM-5:30PM (10 Hrs.).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MA, 1/5/2007

MAURY AUDET
PATENT EXAMINER